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Vaccine 41 (2023) 1916–1924

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Predictors of COVID-19 vaccine uptake among people who inject drugs

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ARTICLE INFO

Article history:
Received 1 July 2022
Received in revised form 21 December 2022
Accepted 18 January 2023
Available online 23 January 2023

Keywords:
COVID-19
Substance use
People who inject drugs
COVID-19 vaccines
Health insurance

ABSTRACT

Introduction: We studied characteristics of COVID-19 vaccination uptake among people who inject drugs (PWID).
Methods: Participants aged ≥18 years who injected drugs ≤1 month ago were recruited into a community-based cohort from October 2020 to September 2021 in San Diego, California Poisson regression identified correlates of having had ≥1 COVID-19 vaccine dose based on semi-annual follow-up interviews through March 15, 2022.
Results: Of 360 participants, 74.7% were male, mean age was 42 years; 63.1% were Hispanic/Mexican/Latinx. More than one-third had ≥1 co-morbidity. HIV and HCV seroprevalence were 4.2% and 50.6% respectively; 41.1% lacked health insurance. Only 37.8% reported having ≥1 COVID-19 vaccine dose. None received ≥3 doses. However, of those vaccinated, 37.5% were previously unwilling/unsure about COVID-19 vaccines. Believing COVID-19 vaccines include tracking devices (adjusted incidence rate ratio [aIRR]: 0.62; 95% CI: 0.42,0.92) and lacking health insurance (aIRR: 0.60; 95% CI: 0.40,0.91) were associated with approximately 40% lower COVID-19 vaccination rates). Ever receiving influenza vaccines (aIRR: 2.16; 95%CI: 1.46, 3.20) and testing HIV-seropositive (aIRR: 2.51; 95% CI: 1.03, 6.10) or SARS-CoV-2 RNA-positive (aIRR: 1.82; 95% CI: 1.05, 3.16) independently predicted higher COVID-19 vaccination rates. Older age, knowing more vaccinated people, and recent incarceration were also independently associated with higher COVID-19 vaccination rates.
Conclusions: One year after COVID-19 vaccines became available to U.S. adults, only one third of PWID had received ≥1 COVID-19 vaccine dose. Multi-faceted approaches that dispel disinformation, integrate public health and social services and increase access to free, community-based COVID-19 vaccines are urgently needed.

1. Introduction

People with opioid use disorder, including people who inject drugs (PWID), appear to be at higher risk of SARS-CoV-2 infection [1] and more severe COVID-19 complications due to substantial comorbidities (e.g., chronic kidney, liver and lung diseases)[2–5], underscoring the need to ensure that they receive COVID-19 vaccinations. However, this population has historically had low healthcare utilization due to lack of health insurance and transportation, stigma and medical mistrust [6,7].

Low uptake of COVID-19 vaccines is a major contributor to higher morbidity and mortality [8]. COVID-19 vaccines became available to the adult U.S. population in early 2021, with recommendations from the U.S. Centers for Disease Control and Prevention (CDC) defining primary series completion as receipt of two vaccine doses for Pfizer-BioNTech®, Moderna® or unspecified U.S.-authorized or approved mRNA COVID-19 vaccines, or one dose for the Janssen® vaccine [9]. In Fall, 2021, the CDC began recommending boosters for individuals who were older, immunosuppressed, had underlying medical conditions or were deemed at higher SARS-CoV-2 risk from occupational or institutional settings [10].

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https://doi.org/10.1016/j.vaccine.2023.01.042
0264-410X/

Studies of COVID-19 vaccine uptake among people who use drugs are sparse. Among PWID attending a syringe services program (SSP) in Oregon, only 10% had received at least one COVID-19 vaccine dose by June 2021 [11]; however, 68% of PWID had received at least one COVID-19 dose in a longstanding cohort of PWID in Baltimore, MD by the same date [12]. In a national survey conducted among Australian SSP attendees in 2021, 49% reported having received at least one COVID-19 vaccine dose, which was significantly lower than the general population [13]. We previously reported that 36% of PWID living in San Diego and Tijuana tested SARS-CoV-2 seropositive but only 7.6% had received ≥1 COVID-19 vaccine dose by September 1, 2021 [1]. In the same sample, nearly one-third were hesitant about COVID-19 vaccination, which was significantly associated with younger age, having more comorbidities, low perceived threat, endorsing COVID-19 disinformation (e.g., conspiracy theories) and obtaining most COVID-related information from social media [14]. Since attitudes and intentions do not necessarily translate to enacted behaviors, we conducted a prospective analysis to identify predictors of COVID-19 vaccine uptake among the sample of PWID residing in San Diego County, California to inform future vaccination approaches.

2. Methods

2.1. Study sample

Adults aged ≥18 years or older who injected drugs within the last month and lived in San Diego County or Tijuana were recruited into a longitudinal cohort study using street outreach in a mobile van. A short screener was used to identify participants who were eligible for study participation, as previously described [1]. Analyses were restricted to San Diego County residents who were included in a RADxUP consortium-funded study, involving either a supplemental survey or ≥1 follow-up visit before March 15, 2022 where COVID-19 vaccine-related topics were assessed. We censored this analysis on March 15, 2022 as this was prior to the initiation of a RADxUP intervention to improve COVID-19 vaccination uptake among PWID in San Diego. Cohort participants living in Tijuana were also excluded since they were subjected to a pop-up COVID vaccine program that significantly improved vaccine uptake [15].

2.2. Measures

Participants provided written informed consent that was obtained after the nature and possible consequences of the study has been fully explained. After providing consent, participants underwent interviewer-administered surveys in English or Spanish using computer assisted personal interviewing. Baseline surveys assessed socio-demographics, chronic health conditions (e.g., diabetes, asthma, hypertension, chronic obstructive pulmonary disease [COPD]), and lifetime and past-six-months experiences of homelessness, incarceration, use of specific drugs, utilization of healthcare and substance use treatment services and SSPs.

To reduce participant burden for the initial visit, we administered a supplemental survey approximately one week later including measures on COVID-19 related beliefs, potential exposures and protective behaviors (e.g., social distancing, masking, COVID-19 testing), and perceived impacts of COVID-19 on income, housing, and food insecurity [16]. Perceived threat of COVID-19 was assessed by asking how worried participants were about getting COVID-19 on a ten point scale [17]. Surveys also assessed sources of COVID-19 information, believing COVID-19 misinformation (i.e., false information spread *without* malicious intent) and disinformation (i.e., false information spread *with* malicious intent) [14], and lifetime receipt of influenza vaccination. Since COVID-19 measures were added after the supplemental survey had already been introduced, participants who had already been administered this survey answered these questions at their next semi-annual visit (i.e., Visit 2).

We asked if participants had ever received a COVID-19 vaccine, and if so, how many doses they had received, dates and locations where doses were received, and the name of the manufacturer, if known. Among unvaccinated participants, interviewers read out a list of potential reasons for COVID-19 vaccine hesitancy based on questions developed by the RADxUP consortium [18], with "other" responses recorded verbatim.

We re-assessed the above measures at semi-annual follow-up visits. Baseline data (n = 360) were collected between Oct 28, 2020 and Oct 25, 2021, supplemental survey data (n = 360) were collected between Nov 05, 2020 and Nov 15, 2021; visit 2 data (n = 305) were collected between 05/07/21 and 03/10/22 and visit 3 data (n = 113) between 12/06/21 and 03/15/22. Participants received $20 USD compensation for each baseline, supplemental and follow-up surveys. We obtained institutional review board approval through the University of California San Diego (UCSD) Office of IRB Administration (OIA) (Project #191390).

2.3. SARS-CoV-2 serology and RNA-PCR

At baseline and the first semi-annual follow-up interview, we collected blood samples by venipuncture to test for SARS-CoV2 antibodies. Sera were batched and tested weekly by Genalyte® (San Diego, CA) using their Maverick™ Multi-Antigen Serology Panel that detects IgG and IgM antibodies to five SARS-CoV-2 antigens [19]. Study staff showed participants how to self-collect anterior nasal swabs in their presence which were placed in viral transport media and shipped to the San Diego Center for AIDS Research (CFAR) laboratory where SARS-CoV2 RT-PCR was conducted using a pooling approach based on the Fluxergy system® (Irvine, CA).

2.4. HIV and HCV serology

At baseline and semi-annually, we conducted serological rapid HIV and HCV tests using the Miriad® HIV/HCV Antibody InTec® Rapid Anti-HCV Test (Avantor, Radnor, PA). Reactive and indeterminate tests underwent a second rapid test with Oraquick® HIV or Oraquick® HCV, respectively (Orasure, Bethlehem, PA). HIV-seropositive specimens were confirmed by Western Blot at the San Diego CFAR. Participants testing seropositive were referred to local healthcare providers.

2.5. Statistical analysis

For the purpose of this analysis, the main outcome was reporting having received ≥1 COVID-19 vaccine dose. COVID-19 vaccines became available in California on April 15, 2021 [20].

We compared characteristics of participants who received ≥1 dose of a COVID-19 vaccine and those who had not using Mann-Whitney U tests for continuous variables and Chi-square or Fisher's Exact tests for categorical variables. Socio-demographic, substance use and health conditions data were drawn from the baseline survey, whereas COVID-19 related data were drawn from the first survey when this data became available for each participant (i.e., either the supplemental or visit 2). We considered statistical significance to be met if confidence intervals did not cross the null value.

To identify predictors of having received ≥1 dose of a COVID-19 vaccine, univariable and multivariable Poisson regressions with robust standard error estimation via generalized estimating equations were conducted with an offset for the natural logarithm of

time spent at risk, calculated as number of days between dates when COVID-19 vaccination was first available and the dates of first self-reported vaccination or the end of observation. Our overall modeling approach was based on a "purposeful selection of variables" strategy, introduced by Hosmer and Lemeshaw [21,22], where subject matter significance, relationships among the independent variables (e.g., correlations, confounding, and interactions) and statistical significance were taken into consideration. Variables used in the univariable models were selected based on previous research findings, subject-matter knowledge and the assumption that they might have played a causal role on the outcome. Based on each variable's effect size on the outcome in conjunction with a liberal level of statistical significance of 0.10, we narrowed down variables to consider in the multivariable model. Variables in the final model were assessed for potential confounding, multi-collinearity and potential two-way interactions.

3. Results

3.1. Sample characteristics

Of 382 cohort participants, 360 completed both baseline and supplemental surveys including questions on COVID-19 vaccination prior to March 15, 2022 and were thus eligible for analysis. - Twenty-two (5.7%) were excluded either because their last survey was prior to when COVID-19 vaccination questions introduced during follow-up (n = 19) or they did not answer these questions (n = 3).

As shown in Table 1, the analytic sample completed on average 2.2 visits (standard deviation [SD] = 0.7). Most were male (74.7%) and Hispanic/Latinx/Mexican (63.1%). Mean age and years of education were 42.5 ([SD] = 10.9) and 10.8 years (SD = 3.0), respectively. At baseline, 42.2% reported experiencing homelessness and 10.6% were incarcerated during the previous 6 months. During at least one of their visits, 41.1% reported lacking health insurance.

Considering health indicators, only 40% had any kind of SARS-CoV-2 test prior to enrolment, but 37.7% tested SARS-CoV-2 seropositive at baseline and 1.7% tested SARS-CoV-2 RNA-positive at baseline or visit 2. Over one-third (35.3%) reported ≥1 co-morbid condition (i.e., hypertension, COPD, diabetes, asthma). Baseline HIV and HCV seroprevalence were 4.2% and 40.8%, with 46.7% and 51.4% of these individuals being previously unaware of their serostatus, respectively. Half (51.4%) had ever received influenza vaccinations.

Compared to the analytic sample, the 22 excluded participants were significantly less likely to be Hispanic/Latino/Mexican (36.4% vs. 63.1%, p = 0.02) and more likely to report past six-month incarceration (27.3% vs. 10.6%; p = 0.03) and social distancing during the pandemic (82% vs. 32%; p < 0.001).

3.2. COVID-19 vaccine uptake and vaccine hesitancy

Of the 360 participants, 136 (37.8%) reported having had ≥1 COVID-19 vaccine dose, of whom 45% reported this at the baseline survey. Of these 136 participants, 123 (90.4%) knew what type of vaccine they received. Of these, 51 (41.5%) reported either the Moderna® or Pfizer® vaccines, among whom 37 (72.6%) reported receiving a second dose that completed their primary vaccine series; 71 (57.7%) reported receiving Janssen® vaccine, constituting the primary vaccine series. Finally, of 13 participants who did not recall which COVID-19 vaccine(s) they received (n = 9) or had their last interview prior to the introduction of questions on vaccine manufacturers (n = 4), 6 (46.2%) received two doses and can be assumed to have completed their primary series, 6 (46.2%) received a single dose of an unknown type, and one did not remember how many doses they received. Overall, 121/360 (33.7%) would have completed their vaccine series considering the most conservative scenario where the seven participants with unknown vaccine types are considered to have completed their vaccine series, whereas 114/360 (31.7%) would have completed their vaccine series under the worst-case scenario. None reported having received ≥3 doses of any COVID-19 vaccine.

Of the 62 participants who were asked about their vaccination location, responses included clinics or doctor's offices (39%), health fairs or drive-throughs (34%), other research studies (10%), pharmacies (8%), drug treatment programs (3%), and jail/prison (3%). Of 80 vaccinated participants who previously answered questions on vaccine hesitancy, 37.5% previously expressed being unwilling or unsure about having received COVID-19 vaccines.

Among the 224 participants who remained unvaccinated, 35.7% reported that they were not interested, 13.4% were unsure and 50.9% were willing to be vaccinated. Among remaining unvaccinated participants, the most common reasons were: "I don't trust that the vaccine will be safe" (40%), "I don't like shots/needles" (16%), "I don't think vaccines work very well" (13%) and "I don't know enough about how COVID vaccines work" (10%), not trusting the government (5%) and concern about side effects (4%).

3.3. Factors associated with COVID-19 vaccine uptake in Univariate Analyses

As seen in Table 2, younger participants, as well as Hispanic/Mexican/Latinx participants were less likely to have had ≥1 dose of a COVID-19 vaccine. Considering behavioral characteristics, higher vaccination rates were observed among participants reporting more years of injection drug use, those who drank more alcohol, and those who had been incarcerated in the last six months (see Table 3).

Health-related factors that were more likely to be reported among participants who received at least one COVID-19 vaccine dose included having ≥1 chronic health condition (e.g., hypertension or heart problems). Testing HIV-seropositive was marginally associated with higher COVID-19 vaccination rates. Ever having received influenza vaccine predicted higher COVID-19 vaccination rates, whereas those lacking health insurance during follow-up had lower vaccination rates.

Higher COVID-19 vaccination rates were reported among participants who knew more people who received COVID-19 vaccines or who died of COVID-19 and those who received COVID-19 testing outside of the study. Participants who engaged in protective behaviors such as social distancing and wearing facemasks had higher vaccination rates. Those who obtained most of their COVID-19 information from liberal-leaning sources (e.g., MSNBC, NPR, CNN) or health professionals had higher vaccination rates, whereas those whose main sources were friends were less likely.

Considering COVID-19 related beliefs, 26.1% believed that COVID-vaccines included a tracking device (Table 1). Those endorsing this belief (i.e., a measure of disinformation), and those who did not think that many thousands of people had died from COVID-19 (i.e., a measure of misinformation) were less likely to have had ≥1 dose of a COVID-19 vaccine.

Suspecting that they already had COVID-19, having been exposed to someone who tested positive, and having been hospitalized for COVID-19 were not associated with COVID-19 vaccination. Although testing SARS-CoV-2 seropositive was not associated with subsequent COVID-19 vaccination, testing SARS-CoV-2 RNA-positive at baseline or visit 2 was significant after controlling for age (aIRR: 2.08; 95% CI: 1.01, 4.32).

Table 1
Characteristics of PWID in San Diego, CA who had ≥1 COVID-19 vaccine dose versus Unvaccinated PWID (N = 360).

Participants' Characteristics	Had ≥1 COVID-19 vaccine dose N = 136	Unvaccinated N = 224	Total N = 360	P[p]
Mean # of study visits completed (SD)	2.2(0.7)	2.1(0.7)	2.2(0.7)	0.12
Socio-demographics[b]				
Sex at birth (male)	106(77.9%)	163(72.8%)	269(74.7%)	0.27
Mean Age (SD)	44.6(10.8)	41.2(10.8)	42.5(10.9)	**0.01**
Hispanic/Latino/Mexican	76(55.9%)	151(67.4%)	227(63.1%)	**0.03**
Speaks English	131(96.3%)	218(97.3%)	349(96.9%)	0.59
Born in the US	109(80.1%)	167(74.6%)	276(76.7%)	0.22
Mean # of years education (SD)	10.9(3.0)	10.8(3.0)	10.8(3.0)	0.33
Married or Common law	26(19.1%)	32(14.3%)	58(16.1%)	0.23
Average monthly income < 500 USD	39(28.7%)	86(38.4%)	125(34.7%)	0.06
Has a smart phone or access to a computer	65(48.1%)	92(41.1%)	157(43.7%)	0.19
Potential COVID-19 Exposures				
Experienced Homelessness*	60(44.1%)	92(41.1%)	152(42.2%)	0.57
Mean no. of hours spent on the street (SD)*	15.3(7.8)	15.3(7.4)	15.3(7.5)	**0.90**
Lacks health insurance at least at one visit	39(28.7%)	109(48.7%)	148(41.1%)	**<0.001**
Incarcerated*	21(15.6%)	17(7.6%)	38(10.6%)	**0.02**
Mean no. of people in the same household (SD)*	6.8(42.9)	4.1(9.3)	5.1(27.3)	0.90
Engaged in sex work*	10(7.4%)	18(8.0%)	28(7.8%)	0.81
Client of sex worker*	4(2.9%)	9(4.0%)	13(3.6%)	0.77
Income worse since COVID began	80(59.7%)	135(60.8%)	215(60.4%)	0.84
Low/very low food security since COVID began	102(75.0%)	178(79.5%)	280(77.8%)	0.32
Substance Use[b]				
Higher risk drinking	20(14.7%)	19(8.5%)	39(10.8%)	0.07
Smokes cigarettes	116(85.3%)	199(88.8%)	315(87.5%)	0.32
Smoked or vaped marijuana*	82(60.3%)	132(58.9%)	214(59.4%)	0.80
Smoked/snorted/inhaled/vaped/methamphetamine*	96(70.6%)	147(65.6%)	243(67.5%)	0.33
Smoked/snorted/inhaled crack or powder cocaine*	23(16.9%)	26(11.6%)	49(13.6%)	0.15
Smoked/snorted/inhaled/vaped either heroin or fentanyl*	59(43.4%)	86(38.4%)	145(40.3%)	0.35
Injected methamphetamine*	73(53.7%)	104(46.4%)	177(49.2%)	0.18
Injected cocaine*	16(11.8%)	18(8.0%)	34(9.4%)	0.27
Injected either heroin or fentanyl*	120(88.2%)	203(90.6%)	323(89.7%)	0.47
Mean no. of years of injection drug use (SD)	22.1(12.6)	18.9(12.3)	20.1(12.5)	**0.01**
Mean # of times injected drugs per day (SD)*	2.0(1.5)	1.9(1.5)	1.9(1.5)	0.70
Visited shooting galleries*	3(2.2%)	4(1.8%)	7(1.9%)	1.00
Receptive needle sharing*	52(38.2%)	102(45.5%)	154(42.8%)	0.17
Crossed border to inject drugs*	62(45.6%)	123(54.9%)	185(51.4%)	0.09
Health Conditions[b]				
Tested HIV-seropositive	8(5.9%)	7(3.1%)	15(4.2%)	0.20
Tested HCV-seropositive	51(37.8%)	95(42.6%)	146(40.8%)	0.37
Has diabetes	7(5.1%)	11(4.9%)	18(5.0%)	1.00
Has asthma or other lung problems	10(7.4%)	22(9.8%)	32(8.9%)	0.42
Has hypertension	22(16.2%)	18(8.0%)	40(11.1%)	**0.02**
Has heart problems	6(4.4%)	2(0.9%)	8(2.2%)	**0.05**
Has at least one chronic illness	57(41.9%)	70(31.3%)	127(35.3%)	**0.04**
Mean no. of chronic conditions (excluding seasonal allergies and acne/skin problems) (SD)	0.7(1.1)	0.5(1.1)	0.6(1.1)	**0.02**
Protective behaviors during the COVID-19 Pandemic[f]				
Practiced Social Distancing	54(39.7%)	61(27.2%)	115(31.9%)	**0.01**
Isolated or quarantined itself	10(7.4%)	16(7.1%)	26(7.2%)	1.00
Wore face mask	117(86.0%)	181(80.8%)	298(82.8%)	0.20
Increased handwashing/sanitizer	39(28.7%)	59(26.3%)	98(27.2%)	0.63
Engaged in at least 1 protective behavior	127(93.4%)	201(89.7%)	328(91.1%)	0.24
Enrolled in methadone/buprenorphine program*	11(8.1%)	19(8.5%)	30(8.3%)	
COVID-19-related disinformation (i.e. endorsement of conspiracy theories)				
Thinks that the pharmaceutical industry created the COVID-19 virus	51(37.5%)	109(48.7%)	160(44.4%)	**0.04**
Thinks COVID-19 was created by the Chinese government as a biological weapon	65(47.8%)	116(51.8%)	181(50.3%)	0.46
Thinks that vaccines given to children for diseases like measles and mumps cause autism	75(55.1%)	130(58.0%)	205(56.9%)	0.59
Thinks that COVID-19 vaccines being offered to 'people like me' are not as safe	49(36.0%)	73(32.6%)	122(33.9%)	0.50
Thinks COVID-19 vaccines include a tracking device	28(20.6%)	66(29.5%)	94(26.1%)	0.06
Thinks COVID-19 vaccines could change their DNA	34(25.0%)	70(31.3%)	104(28.9%)	0.20
Mean no. of conspiracy items that they believe (out of 6)(SD)	2.2(1.9)	2.5(1.9)	2.4(1.9)	0.17
COVID-19-related misinformation (i.e. incorrect knowledge items)[f]				
Does NOT think that the virus that causes COVID-19 can be easily spread from one person to another	28(20.6%)	59(26.3%)	87(24.2%)	0.22
Does NOT think that many thousands of people have died from COVID-19	13(9.6%)	39(17.4%)	52(14.4%)	**0.04**
Thinks that most people already have immunity to COVID-19	87(64.0%)	144(64.3%)	231(64.2%)	0.95
Thinks that you can tell someone has COVID-19 by looking at them	27(19.9%)	48(21.4%)	75(20.8%)	0.72
Thinks that there are effective treatments for COVID-19 that can cure most people	105(77.2%)	172(76.8%)	277(76.9%)	0.93
Thinks that having COVID-19 is about as dangerous as having the flu	76(55.9%)	114(50.9%)	190(52.8%)	0.36
Does NOT think that COVID-19 vaccines are safe for pregnant women	83(61.0%)	151(67.4%)	234(65.0%)	0.22
Most important source of COVID-19-related information[f]				
Friends [Y1]	34(25.6%)	76(35.7%)	110(31.8%)	**0.05**

(*continued on next page*)

Table 1 (*continued*)

Participants' Characteristics	Had ≥1 COVID-19 vaccine dose N = 136	Unvaccinated N = 224	Total N = 360	P[p]
Doctors/health professionals [Y1]	18(13.5%)	14(6.6%)	32(9.2%)	**0.03**
Liberal TV/radio [Y1]	16(12.0%)	23(10.8%)	39(11.3%)	0.72
Social media [Y1]	25(18.8%)	34(16.0%)	59(17.1%)	0.50
Additional COVID-19-related experiences[f]				
Knows someone who died of COVID-19	51(37.5%)	59(26.3%)	110(30.6%)	**0.03**
Mean for: On a scale of 1 to 10, how worried are you of getting COVID-19 (SD)	4.5(3.0)	4.5(3.0)	4.5(3.0)	0.89
Mean no. of people they know who had a COVID-19 vaccine (SD)	22.2(87.7)	8.0(13.4)	13.4(55.2)	**<0.001**
Thinks they had COVID-19	28(20.6%)	43(19.2%)	71(19.7%)	0.75
Had a COVID-19 test prior to joining study	68(50.0%)	76(33.9%)	144(40.0%)	**<0.001**
Exposed to somebody diagnosed with COVID-19	11(8.1%)	19(8.5%)	30(8.3%)	0.90
Currently has ≥1 COVID-19 symptom	31(22.8%)	47(21.0%)	78(21.7%)	0.69
SARS-CoV-2 seropositive [Y2]	46(34.6%)	85(38.8%)	131(37.2%)	0.43
SARS-CoV-2 RNA+ (baseline or visit 2) [Y3]	4(3.0%)	2(0.9%)	6(1.7%)	0.20
Hospitalized for COVID-19	4(2.9%)	5(2.2%)	9(2.5%)	0.68
Ever had influenza vaccine	91(66.9%)	94(42.0%)	185(51.4%)	**<0.001**

[b] Baseline characteristics, unless noted otherwise.
[f] Assessed at the first available visit.
[*] past 6 months; Missing values.
[Y1] n = 14.
[Y2] n = 8.
[Y3] n = 3; Boldface indicates statistical significance (p < 0.05).
[p] P-values from Mann-Whitney tests (used for continuous variables), Chi-square tests (used for binary variables with cell values > 5), Fisher's exact tests (used for binary variables with cell values<=5).

3.4. Independent predictors of COVID-19 vaccine uptake

As shown in Table 3, factors independently associated with having had ≥1 dose of a COVID-19 vaccine included older age (Adjusted Incidence Rate Ratio [aIRR]: 1.29 per ten-year increase (95% Confidence Interval [CI]: 1.11, 1.51) and knowing more people who had received COVID-19 vaccines (aIRR: 1.02 per 10 persons; 95% CI: 1.01, 1.03). Ever receiving influenza vaccines, testing HIV-seropositive and SARS-CoV-2 RNA-positive were also independently associated with having had ≥1 dose of COVID-19 vaccine (aIRR: 2.16; 95%CI: 1.46, 3.20 and aIRR: 2.51; 95% CI: 1.03, 6.10 and aIRR: 1.82; 95% CI: 1.05, 3.16, respectively). Having been incarcerated in the last six months was also independently associated with having had also predicted ≥1 dose of COVID-19 vaccine (aIRR: 1.80; 95% CI: 1.07, 3.02). Finally, not having health insurance during at least one study visit and believing that COVID-19 vaccines include a tracking device were both independently associated with 40% lower rates of having had ≥1 dose of a COVID-19 vaccine (aIRR: 0.60; 95% CI: 0.39, 0.91 aIRR: 0.62; 95% CI: 0.42, 0.92, respectively). Adjustment for other sociodemographic factors such as sex or race/ethnicity did not significantly alter parameter estimates. No significant interactions were observed.

4. Discussion

Approximately one year after COVID-19 vaccines first became available to the general U.S. population, only one-third of PWID in San Diego County had received at least one COVID-19 vaccine dose and none had received boosters that have been shown to offer greater immunologic protection against several SAR-CoV-2 variants [23]. In contrast, over 80% of adult San Diego County residents had received at least two Pfizer or Moderna COVID-19 doses or one Janssen COVID-19 vaccine dose by the end of the observation period on March 15, 2022 [24]. COVID-19 vaccine coverage in our study was much lower than that reported in the aforementioned studies of PWID in Baltimore [12] and Australia [13], but was higher than a study of PWID attending a SSP in Oregon [11]. Although some health agencies monitor vaccine coverage by race/ethnicity, geographic disparities and experiences of homelessness, our findings suggest that it is critical to understand and address barriers to vaccine equity.

We identified several facilitators and barriers to COVID-19 vaccination than can inform health policies and program planning for this marginalized population. One quarter of participants believed that COVID-19 vaccines contained a tracking device, an example of disinformation perpetuated on social media [25], and COVID-19 vaccination rates were 40% lower for those endorsing this belief. This finding is consistent with a study of the U.S. general population which reported that those who believed COVID-19 conspiracy theories were significantly less likely to receive COVID-19 vaccines [26]. We previously found that endorsing COVID-19 disinformation, including the belief that COVID-19 vaccines contained tracking devices, was independently associated with COVID-19 vaccine hesitancy in a cross-sectional analysis that included the subgroup of PWID who resided in San Diego, CA, as well as those living in nearby Tijuana, Mexico [14]. In a qualitative study conducted within the same PWID cohort in San Diego, unreliable sources of COVID-19-related information were found to reinforce medical and institutional mistrust [27]. A study of PWID in Baltimore found that distrust of COVID-19 vaccines independently predicted not having received a COVID-19 vaccine [12].

An important finding was that more than one third of vaccinated PWID in our study had previously expressed COVID-19 vaccine hesitancy. This indicates that attitudes can and do change and offers hope that interventions which increase health literacy and dispel myths about vaccines could increase COVID-19 vaccine uptake among PWID who are initially hesitant. Our studies extend research which found that 58% and 48% of unvaccinated PWID in Oregon and Australia were vaccine hesitant [11,28] respectively, whose concerns about safety and side effects were also similar. Since we also found that participants who knew more people who had received COVID-19 vaccines had greater vaccine uptake, public health messaging for PWID should focus on dispelling conspiracy theories and fostering health literacy by enlisting peers, trusted community opinion leaders and outreach workers [28]. In a recent study in Tijuana, significantly higher COVID-19 vaccination rates occurred among PWID who attended a "pop-up" vaccine clinic that was staffed by medical professionals possessing experience working with substance using populations [15]. Similar

Table 2
Factors associated with having had ≥1 COVID-19 vaccine dose among PWID in San Diego, CA: Univariate Analyses.

Participants' Characteristics	Univariate IRR (95% CI)
No. of study visits completed	0.87 (0.68,1.11)
Socio-demographics[b]	
Sex at birth (male)	1.18 (0.78,1.80)
Age[Z]	**1.27 (1.09,1.48)**
Hispanic/Latino/Mexican	**0.65 (0.46,0.91)**
Speaks English	0.79 (0.33,1.86)
Born in the US	1.33 (0.86,2.05)
Years of education[¥]	1.03 (0.97,1.09)
Married or common law	1.23 (0.81,1.87)
Monthly income < 500 USD	0.77 (0.53,1.13)
Has a smart phone or access to a computer	1.33 (0.95,1.87)
Experienced Homelessness[*]	1.08 (0.77,1.52)
No. of hours spent on the street[*]	1.00 (0.97,1.02)
Lacks health insurance at least at one visit	**0.45 (0.31,0.65)**
Incarcerated[*P]	**2.05 (1.29,3.26)**
No. of people in the same household[*]	**1.01 (1.00,1.01)**
Engaged in sex work[*]	0.86 (0.47,1.57)
Client of sex worker[*]	0.72 (0.29,1.80)
Income worse since COVID began	0.86 (0.61,1.23)
Low or very low food security since COVID began	0.78 (0.51,1.18)
Substance Use[b]	
Higher risk drinking	**1.72 (1.08,2.73)**
Smokes cigarettes	0.76 (0.47,1.22)
Smoked or vaped marijuana[*]	1.10 (0.78,1.57)
Smoked/snorted/inhaled/vaped methamphetamine[*]	1.30 (0.90,1.89)
Smoked/snorted/inhaled crack or powder cocaine[*]	**1.63 (1.06,2.52)**
Smoked/snorted/inhaled/vaped either heroin or fentanyl[*]	1.28 (0.91,1.81)
Injected methamphetamine[*]	1.21 (0.86,1.71)
Injected cocaine[*]	1.64 (0.98,2.75)
Injected heroin or fentanyl[*]	0.85 (0.52,1.38)
No. of years of injection drug use[¥]	**1.02 (1.00,1.03)**
No. of times injected drugs per day[*]	1.03 (0.92,1.15)
Visited shooting galleries[*]	1.00 (0.36,2.78)
Receptive needle sharing[*]	0.79 (0.55,1.12)
Crossed border to inject drugs[*]	**0.67 (0.48,0.95)**
Health Conditions[b]	
Tested HIV-seropositive	2.15 (0.86,5.39)
Tested HCV-seropositive	0.93 (0.65,1.31)
Has diabetes	1.30 (0.59,2.85)
Has asthma or other lung problem	0.94 (0.47,1.88)
Has hypertension	**1.92 (1.17,3.14)**
Has heart problems	**2.79 (1.53,5.11)**
Has at least one chronic illness	**1.49 (1.06,2.11)**
No. of chronic conditions (excluding seasonal allergies and acne/skin problems	**1.17 (1.02,1.33)**
Protective behaviors during the COVID-19 Pandemic[f]	
Practiced social distancing[P]	**1.66 (1.18,2.35)**
Isolated or quarantined itself	1.31 (0.70,2.46)
During the COVID pandemic: Wore face mask	1.42 (0.88,2.31)
During the COVID pandemic: Increased handwashing/sanitizer	1.10 (0.75,1.60)
During the COVID pandemic: Engaged in at least 1 protective behavior	1.48 (0.75,2.93)
Enrolled in methadone/buprenorphine program[*]	1.13 (0.61,2.11)
***COVID-19-related disinformation* (i.e. *endorsement of conspiracy theories*)**[f]	
Thinks that the pharmaceutical industry created the COVID-19 virus	0.77 (0.54,1.10)
Thinks that COVID-19 was created by the Chinese government as a biological weapon	0.91 (0.64,1.27)
Thinks that vaccines given to children for diseases like measles and mumps cause autism	0.97 (0.69,1.36)
Thinks that COVID-19 vaccines being offered to 'people like me' are not as safe as other COVID vaccines	1.09 (0.77,1.55)
Thinks that COVID-19 vaccines include a tracking device	**0.66 (0.44,1.00)**
Thinks that COVID-19 vaccines could change their DNA	0.80 (0.55,1.18)
No. of conspiracy items that they believe (out of six)	0.95 (0.87,1.04)
***COVID-19-related misinformation* (i.e. *incorrect knowledge items*)**[f]	
Does NOT think the virus that causes COVID-19 can be easily spread from one person to another	0.82 (0.53,1.25)
Does NOT think that many thousands of people have died from COVID-19	**0.57 (0.32,1.00)**
Thinks that most people already have immunity to COVID-19	1.00 (0.70,1.41)
Thinks that you can tell someone has COVID-19 by looking at them	0.93 (0.61,1.42)
Thinks that there are effective treatments for COVID-19 that can cure most people	1.05 (0.70,1.58)
Thinks that having COVID-19 is about as dangerous as having the flu	1.17 (0.83,1.65)
Does NOT think that COVID vaccines are safe for pregnant women	0.92 (0.65,1.31)
Most important source of COVID-19 information to the study participant: Friends[Y1]	**0.59 (0.40,0.87)**
Most important source of COVID-19 information to the study participant: Doctors/health professionals[Y1P]	**1.97 (1.19,3.27)**
Most important source of COVID-19 information to the study participant: Liberal TV/radio[Y1]	1.30 (0.75,2.25)
Most important source of COVID-19 information to the study participant: Social media[Y1]	1.20 (0.78,1.86)
Additional COVID-19-related experiences[f]	
Knows someone who died of COVID-19	1.44 (1.01,2.04)
On a scale of 1 to 10, how worried are you of getting COVID-19[¥]	**0.99 (0.94,1.05)**

(*continued on next page*)

Table 2 (*continued*)

Participants' Characteristics	Univariate IRR (95% CI)
No. of people they know who have had a COVID-19 vaccine[Z]	**1.03 (1.02,1.04)**
Thinks they had COVID-19	1.05 (0.70,1.59)
Had a COVID-19 test prior to joining the study	**1.95 (1.39,2.74)**
Exposed to somebody diagnosed with COVID-19	1.02 (0.57,1.84)
Currently has- ≥1 COVID-19 symptom	1.24 (0.83,1.86)
SARS-CoV-2 seropositive[Y2]	0.87 (0.60,1.25)
SARS-CoV-2 RNA+ (baseline or visit 2)[Y3]	1.66 (0.79,3.47)
Hospitalized for COVID-19	1.21 (0.50,2.90)
Ever had influenza vaccine	**2.44 (1.70,3.49)**

[b] Baseline characteristics, unless noted otherwise.
[f] Assessed at the first available visit.
[*] past 6 months; Missing values.
[Y1] n = 14.
[Y2] n = 8.
[Y3] n = 3.
[¥] Per one unit increase.
[Z] Per 10 units increase; Boldface indicates statistical significance ($p < 0.05$) from Wald Chi-Squared tests.

Table 3
Factors Independently Associated with having had ≥1 COVID-19 vaccine dose among PWID in San Diego, CA: Multivariate Analyses.

Baseline Characteristics	Adjusted IRR (95% CI)	P-value[P]
Age (per 10 year increase)	**1.29 (1.11,1.51)**	**0.001**
Number of people they know who have had a COVID-19 vaccine (per every 10 people)	**1.02 (1.01,1.03)**	**<0.001**
Ever had an influenza vaccine	**2.16 (1.46,3.20)**	**0.001**
Incarcerated[*]	**1.80 (1.07,3.02)**	**0.03**
Tested HIV seropositive	**2.51 (1.03,6.10)**	**0.04**
Lacks health insurance at least at one visit	**0.60 (0.39,0.91)**	**0.02**
Thinks that COVID vaccines include a tracking device	**0.62 (0.42,0.92)**	**0.02**
Tested SARS-CoV-2 RNA+ (at baseline or visit 2)	**1.82 (1.05,3.16)**	**0.03**

[*] past 6 months [Z]Per 10 units increase; Boldface indicates statistical significance ($p < 0.05$).
[P] P-values from Wald Chi-Squared tests.

approaches to increase COVID-19 vaccination should be offered at locations where PWID seek services, such as drug treatment programs, SSPs, soup kitchens, homeless shelters and community health fairs.

Our finding that half of unvaccinated participants were interested in being vaccinated also confirms that hesitancy was not the only impediment to COVID-19 vaccination. Despite Medicaid expansion in California, over 40% of our cohort lacked health insurance at least once during the follow-up period, which likely limited their interactions with the healthcare system. Although COVID-19 vaccines were offered for free to all medically-eligible U.S. adults during the study period, marginalized communities may have been unaware of this or experienced other barriers to vaccination. For example, many of our participants lacked government-issued photo identification, which some vaccine clinics required despite this being a known barrier to accessing preventative and other healthcare services [29]. It may be unrealistic to assume that COVID-19 vaccination rates will significantly improve in this population without improving their overall access to health care. The U.S. federal government has not extended emergency COVID-19 funding to ensure that vaccine manufacturers will continue to offer free COVID-19 vaccines for uninsured individuals [30].

Although less than one half of participants had been tested for SARS-CoV-2 prior to enrolment, an encouraging finding was that those testing SARS-CoV-2 RNA-positive at baseline or at their first semi-annual follow-up visit had significantly higher vaccination rates. This finding contrasts our previous study where previously testing SARS-CoV-2 seropositive was not significantly associated with COVID-19 vaccine hesitancy. However, in that study, participants were unaware of their COVID serology results at the time of interview as testing was not done in real time and their SARS-CoV-2 RNA test results were not yet available. Having received a prior COVID-19 test was a significant predictor of COVID vaccination among PWID in Australia [13]. These findings suggest that efforts to expand COVID-19 case-finding for this population could have a positive impact on COVID-19 vaccine coverage.

We also found that ever having received influenza vaccine was significantly associated with COVID-19 vaccination. This is consistent with studies in the U.S. general population suggesting that attitudes about COVID-19 vaccines are correlated with global vaccine acceptance or hesitancy [31,32]. This finding is similar to the Baltimore study which found that PWID who had received influenza vaccine within the last year were more likely to have had at least one COVID-19 vaccine dose and were less vaccine hesitant, [12] which led these authors to conclude that PWIDs' attitudes about vaccines in general are important predictors of vaccine uptake. Only half of our sample reported ever having had an influenza vaccine, indicating that public health initiatives could benefit from integrating vaccination campaigns for COVID-19, influenza, and other vaccine-preventable diseases prevalent among PWID, such Hepatitis A and B [33].

We also found that participants testing HIV-seropositive were twice as likely to have received at least one COVID-19 vaccine dose, which is reassuring because COVID-19 vaccination is highly recommended for immunocompromised persons [34]. HIV-positive PWID were also more likely to have had COVID-19 vaccines in the Baltimore study [12]. Although HIV seroprevalence was low in our study, incidence has been rising among PWID in the Mexico-US border region [35], and among those in Tijuana, most are out of care. This is a worrisome trend since SARS-CoV-2 may

cause more serious disease in HIV-infected persons, especially if they are not virally suppressed [36].

Participants who were recently incarcerated also had higher COVID-19 vaccination rates, but it is not clear if this reflects voluntary or system-mandated vaccination. Although the California Department of Corrections and Rehabilitation mandated that incarcerated people be completely vaccinated against COVID-19 in September 2021, this order did not come into effect until December 2021. Ensuring that incarcerated people are able to freely obtain COVID-19 vaccines is critically important given that COVID-19 outbreaks have been linked to correctional facilities [37]. In our previous study, we found that PWID in the U.S.-Mexico border region who had been recently been incarcerated were more likely to test SARS-CoV-2 seropositive [1]. Given that PWID are in frequent contact with the correctional system, it is equally important that COVID-19 vaccinations are available in post-release settings.

5. Limitations

Limitations of our study include the non-random nature of our sampling due to the criminalized nature of drug use. We relied on self-report for COVID-19 vaccination status and most of the other measures studied, which could be subject to socially desirable responding. However, participant reimbursement was not tied to COVID-19 vaccination responses. Our findings may not be generalizable outside of Southern California or to people who do not inject drugs, and may not be comparable to other time periods in the COVID-19 pandemic. Although our analysis was prospective, most participants contributed data on COVID-19 vaccine experiences and attitudes at only two time points. For the minority of vaccinated participants whose attitudes were reported on visit 2, the short time to vaccination suggests that the interview itself might have affected vaccination rates. We cannot infer that the associations we observed were causal due to potential issues in temporality, the potential for unmeasured confounding, and limited statistical power for some associations.

Finally, we cannot directly compare our findings to those from our previous manuscript on COVID-19 vaccine hesitancy, since the prior analysis included participants from Tijuana and the present analysis focuses only on those residing in San Diego. This is because Tijuana implemented a successful intervention to increase COVID-19 vaccine uptake among marginalized persons [15], and thus the COVID vaccination experiences among PWID in the two cities were no longer comparable.

6. Conclusions

One year after COVID-19 vaccines became available in the U.S., only one-third of PWID had received at least one COVID-19 vaccine dose, which has implications for improving COVID-19 vaccine delivery to this socially marginalized population, and for protecting the health of the general population. Our findings suggest that disparities in COVID-19 burden that have been previously reported [1,4] are exacerbated by disparities in vaccine access.

Since more than one third of vaccinated PWID had previously been hesitant towards COVID-19 vaccines and half of unvaccinated PWID expressed interest in being vaccinated, our results suggest that targeted efforts to thwart disinformation and medical distrust could improve COVID-19 vaccination in this population. Our study and others found greater COVID-19 vaccination uptake in circumstances where PWID have trust in the medical establishment and when they have received preventive services or health care for other conditions [12,13,15,27]. Resources should be allocated to integrate COVID-19 vaccination into programs that are frequented and trusted by PWID, which includes SSPs and other harm reduction programs, homeless shelters, health fairs and drug treatment centers. Our team recently developed a brief, theory-based motivational interviewing intervention to be offered in a RADxUP collaboration with a local SSP to increase COVID-19 vaccine uptake among PWID [38]. Given that California and many other U.S. states have considerably under-spent resources allocated towards COVID-19 disparities [39], the extremely low vaccination rates we observed in a community that is disproportionately Latinx and experiencing a high prevalence of homelessness should be a clarion call to action.

Author Contributions

All authors attest they meet the ICMJE criteria for authorship. CFV was responsible for data collection and translation of survey measures. DA oversaw the data management, programmed study instruments, conducted the data analysis, prepared the results and helped interpret findings. IA programmed study instruments and conducted the data management. SAS conceived the study design and most of the measures, oversaw the analysis, and wrote the manuscript. SAS, TP, DS and ARB interpreted the analysis and its public health implications. All authors reviewed and edited the manuscript.

Data availability

Data will be made available on request.

Declaration of Competing Interest

The authors have no competing interests to declare.

Acknowledgments

The authors gratefully acknowledge Alicia Harvey-Vera for assistance with data collection and Carole Ignacio for SARS-CoV-2 RNA testing. SAS, DA, CFV, IA, TLP, AC, and ARB all report support from the National Institute on Drug Abuse (NIDA) at the National Institutes of Health (NIH) (R01DA049644-S1, R01DA049644-S2 and K01DA043412). SAS, DMS, ARB all report support from the National Institute of Allergy and Infectious Diseases (P30 AI036214). The research presented in this paper is that of the authors and does not reflect the official policy of the NIH. Additionally, grant sponsors had no involvement in the study or the manuscript.

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